

REMARKS

Applicant respectfully requests reconsideration of the present application in view of the foregoing amendments and in view of the reasons that follow.

Claim 34 is currently being amended.

In the Advisory Action of October 8, 2004, the Examiner upheld her previous rejections of claims 1-3, 7, 19-23, 27, 32-35, 39-41 and 57-64 under 35 U.S.C. § 102(e) as being anticipated by U.S. Patent No. 5,503,771, issued to Staley et al.¹ In making these rejections, the Examiner has made a number of inaccurate assumptions and statements which are neither supported by the law nor the prior art upon which the Examiner is relying. Each of these issues are discussed below.

First, the Examiner has continued to cite the Staley et al. reference against the above-referenced claims despite the fact that this reference has absolutely no applicability to the present invention. The Staley et. al. reference is completely unrelated to the tissue augmentation material of the present invention. The “Background of the Invention” of the Staley et al. reference is clear that this particular reference relates to the “production of formed articles such as engine components and superconductive composites” and not tissue augmentation materials. The Staley et al. reference never makes a single mention of tissue augmentation, nor does it ever refer to the injection or implantation of the material into a live body of any sort. In fact, the Background of the Invention makes clear that the Staley et al. reference is directed to the manufacture of engine components, not to tissue augmentation.

Every one of the currently rejected claims, on the other hand, specifically claims and refers to either a tissue augmentation material or a biocompatible composition for augmenting

¹ The Examiner made a number of rejections under 35 U.S.C. § 112, second paragraph. The Examiner also objected to several other claims for various reasons. However, these issues were fully addressed in Applicants’ September 13, 2004 Amendment After Final Rejection. These amendments were acknowledged in Advisory Action issued on October 8, 2004.

tissue. This feature has been consistently ignored by the Examiner when citing the Staley et al. reference.

In ignoring the features and relevance of tissue augmentation in the present claims, the Examiner has apparently concluded that the discussion of tissue augmentation in the preamble of the respective claims is not entitled to any weight. This position is incorrect as a matter of law. The Federal Circuit has repeatedly held that the preamble provides patentable weight and limits the scope of the claimed invention “when they give meaning to the claim and properly define the invention.” *In re Paulson*, 30 F.3d 1475, 1479 (Fed. Cir. 1994) (internal citations omitted). The Federal Circuit has also emphasized that “when the claim drafter chooses to use *both* the preamble and the body to define the subject matter of the claimed invention, the invention is so defined, and not some other, is the one the patent protects.” *Bell Communications Research, Inc. v. Vitalink Communications Corp.*, 55 F.3d 615, 620 (Fed. Cir. 1995).

In the present application, currently rejected claims are replete with such references to tissue augmentation both within the preamble and the body of the claims. (*See, e.g.*, claims 1, 21, 41), showing that there is a clear intention to define the invention in terms of tissue augmentation. In this regard, the current application is similar to the situation presented in *Poly-America, L.P. v. GSE Lining Technology, Inc.*, 383 F.3d (Fed. Cir. 2004). In *Poly America*, the Federal Circuit held that the preamble phrase “blown-film” was a substantive limitation of the patent claims at issue, substantially differentiating the claims over the prior art. In making this determination, the court noted that the specification of the patent-at-issue was “replete with references to the invention as a ‘blown-film’ liner, including the title of the patent itself and the ‘Summary of the Invention,’” while also noting that the phrase was also used repeatedly to describe the preferred embodiments, showing that this feature did not state a purpose or intended use, but instead disclosed an important feature of the claimed invention. *Id. at 1310*. An almost identical situation is presented in the currently rejected claims. The title of the present application (“Tissue Augmentation Material and Method”), the Field of the Invention, the Background of the Invention, the Summary of the Invention, and the Detailed Description of the

Preferred Embodiments refer specifically to tissue augmentation no less than fourteen times, providing clear evidence under *Poly America* that the feature of “tissue augmentation” is entitled to be given patentable weight.

Furthermore, the Federal Circuit has also emphasized that dependence upon a preamble phrase for antecedent basis purposes may limit a claim’s scope because it indicates a reliance on the preamble and the body to define the invention. *Eaton corp. v. Rockwell Int’l Corp.*, 323 F.3d 1332, 1339 (Fed. Cir. 2003); *Catalina Mktg. Int’l v. Coolsavings.com, Inc.*, 289 F.3d 801, 808 (Fed. Cir. 2002). In this case, independent claim 1 clearly refers to the tissue augmentation material in both the body and the preamble, providing yet another clear indication that the feature of a tissue augmentation material is to be given patentable weight.

In addition, the Federal Circuit has also noted that, when a preamble is relied upon during prosecution to distinguish a claimed invention over the prior art, the preamble is transformed into a claim limitation because such reliance indicates the use of the preamble to define, in part, the claimed invention. *Catalina* at 808-809 (citing *Bristol-Myers Squibb Co. v. Ben Venue Labs, Inc.*, 246 F.3d 1368, 1375 (Fed. Cir. 2001)). In Applicants’ May 4, 2004 Amendment and Reply, this type of argument was made and was accepted by the Examiner:

None of the references cited by the Examiner disclose a tissue augmentation material or a biocompatible composition for augmenting tissue, wherein the biomaterial is homogeneously suspended in the carrier both prior to and during the introduction of the composition to a tissue site. Both the Ammann et al. patent and the Hisatuka et al. patent completely fail to disclose, teach or even suggest the homogeneous or uniform suspension of a biomaterial in a gel carrier. In fact, the Hisatuka et al. patent does not even hint at the use of polysaccharide gels in tissue augmentation, which is the focus of the currently pending claims. Regarding the Staley and Chibata et al. patents, neither of these references discloses a biomaterial being homogeneously suspended in a carrier both before and during the introduction of the material into a tissue site, as is specifically required by the claims. The Chibata et al. patent is also completely unrelated to tissue augmentation.

In response to these arguments, the Examiner withdrew all of her rejections based upon all of the cited references except for the Staley et al. reference. Importantly, the Examiner also did not dispute Applicants' position regarding the importance of tissue augmentation in her next communication. These actions fully support the position that the preamble language of a preamble language of a tissue augmentation material has been intended to carry patentable weight.

Given Applicants' clear position that the feature of tissue augmentation is a patentable feature of the currently rejected claims, the Examiner's rejection of these claims cannot stand. As mentioned previously, the Staley et al. reference does not teach, disclose or even suggest a tissue augmentation material of the type described in the pending claims. The Staley et al. reference is instead directed to a completely unrelated field, namely the manufacture of engine components. Furthermore, the Examiner cannot point a single location in the Staley et al. reference that would motivate one skilled in the art of tissue augmentation to even consider the Staley et al. reference as relevant prior art. Because the Staley et al. reference does not teach, disclose or suggest a tissue augmentation material, Applicants respectfully submit that the currently rejected claims are patentable over the Staley et al. reference.

Second, in rejecting claims 1, 19, 20, 21, 39, 40 and 41, the Examiner has admitted that the Staley et al. reference does not "specifically teach gel viscosities in the range of 20,000 to 350,000 centipoise." However the Examiner has instead placed the burden on the Applicants to prove that the prior art does not disclose this viscosity range, essentially blaming the Applicants for "failing to provide guidance regarding concentrations of all possible polysaccharides which would result in viscosities in the range of 20,000 to 350,000" centipoises. Along the same lines, and without any supporting evidence, the Examiner has summarily declared that "any carboxymethylcellulose gel with weight % concentration between 0.25 and 5% will be considered as possessing viscosity in the range of 20,000 to 350,000 centipoise." Furthermore, the Examiner has taken the position that "for all other polysaccharides...any concentration of the polysaccharide will be considered as fulfilling the viscosity requirement."

In response to this position, Applicants respectfully assert that the Examiner's position is completely unsupported by what is presented in the present application, what is discussed in the Staley et al. reference, and what is commonly known in the relevant art. Pages 26 and 27 of the present application make it clear that it is indeed possible for sodium methylcellulose gels to have viscosities outside of a 20,000-350,000 centipoise range. In particular, it is clear that the present invention is directed to this specific range because "[i]t has been found that with gel viscosities below about 20,000 centipoise the particles may not remain in suspension, and with gel viscosities above about 350,000 centipoise, the gel may become too viscous for convenient mixing." This sentence clearly shows that this specific viscosity range was chosen for a specific purpose. Second, it is very well known in the art that viscosities of polysaccharide-containing gels cannot be determined based solely upon the weight percentage of a particular component. Instead, one must look at the ratios and viscosities of each of the individual components. For example, page 27 of the present application notes that, in one embodiment of the present invention, the sodium methylcellulose that is used should have a viscosity of about 1000 to 4000 centipoise. This range of viscosities shows that, for this particular component, the viscosity can vary significantly, and this variance will inherently affect the viscosity of the resulting gel.

Furthermore, the United States Patent Office records are replete with patents and published applications showing polysaccharide gels of the described concentration range where the resulting composition has a viscosity well outside of the 20,000-350,000 centipoise range. For example, U.S. Published Application No. 2001/0003222 clearly discusses the use of a dye having preferably 2% by weight of a thickener such as sodium carboxymethylcellulose, where the dye has a viscosity of preferably as low as two centipoise, well outside of the 1000-4000 centipoise range discussed in the present application for one embodiment of the invention. *See ¶21.* This reference clearly demonstrates that one cannot simply assume a given viscosity given the weight percentage of a single component.

With regard to non-sodium carboxymethylcellulose polysaccharides, there are several other references that discuss gels having a viscosity outside of the specified range. For example

only, Published U.S. Application No. 2004/0224144 clearly discusses the use of carrageenans, alginates, and carboxymethylcellulose gums being used as a thickening agent in a solution having an ultimate viscosity of as low as 2500 centipoise, even when the thickening agent provides between .5 and 2% of the total solution. See ¶¶ 41, 43. This is further evidence that it is wholly improper for the Examiner to “assume” that any polysaccharide gel in the prior art anticipates a claim having a specific viscosity range.

In addition to the above, the Staley et al. reference itself completely undercuts the Examiner’s position that any prior art polysaccharide gel anticipates gels having the cited viscosity range. In particular, column 5, lines 57-64 clearly and unambiguously states:

The suspensions prepared by the present method have a pourable viscosity to enable introduction of the suspension into a mold to produce a formed article. Thus the method is well suited for use in injection molding processes. As used herein, the term "pourable viscosity" refers to viscosities of less than 5,000 centipoise (cp), and more preferably to less than 1,000 cp, and still more preferably to less than about 500 cp, when measured at a shear rate of 9.2 s.sup.-1.

This passage, which comes from the exact same prior art reference which is relied upon by the Examiner, is crystal clear in showing that one cannot make the assumptions that have been made by the Examiner.

In light of the clear refutation of the Examiner’s position concerning applicable viscosity ranges, the Examiner’s rejections based upon the Staley et al. reference cannot stand. As admitted by the Examiner the Staley et al. reference does not disclose a tissue augmentation material having a viscosity between about 20,000 centipoise to about 350,000 centipoise. Furthermore, every reference to viscosity within the Staley et al. patent refers to a viscosity significantly below the minimum threshold of about 20,000 centipoise of the currently rejected claims. As discussed above, the Staley et al. reference is unambiguous in requiring a “pourable viscosity” of less than 5,000 centipoise, and preferably less than 500 centipoise. Furthermore, the Examples presented in the Staley et al. reference discusses suspensions from as low as 5

centipoise (Example 3) to as high as 3,720 centipoise (Example 1). However, the Staley et al. reference clearly does not disclose a specific, higher viscosity range of about 20,000 to about 350,000 centipoise. Instead, the reference consistently teaches away from it by encouraging the use of products having significantly lower viscosities. For all of these reasons, Applicants respectfully submit that the Staley et al. reference does not teach the use of a suspension having a viscosity of between about 20,000 and about 350,000 centipoise.

Third, the August 17, 2004 Official Action included other assumptions in the “Claim Interpretation” Section that require clarification. For example, the Examiner took the position that spherical ceramic particles inherently are substantially non-resorbable. This statement is incorrect. As an example of this fact, Applicants have attached a copy of an Abstract of an article entitled “Resorbable and Nonresorbable Hydroxyapatite Granules as Bone Graft Substitutes in Rabbit Cortical Defects.” This document clearly and unequivocally shows that such ceramic particles can be both resorbable and non-resorbable. The Examiner is therefore not permitted to assume that any such particle is non-resorbable.

The Examiner also claimed that all polysaccharide gels are inherently biocompatible. This statement is incorrect as well. As an example only, the Examiner is directed to the attached article entitled “A Poison Capsule Defense” from the January 11, 2002 edition of Science Magazine. This article clearly discusses the production of a toxic polysaccharide, which is clearly not biocompatible.

Still further, the Examiner has asserted that all polysaccharide gels are lubricous, which ordinarily means having a slippery or smooth quality. However, there are a wide variety of polysaccharide gels which are not commonly thought of as being lubricous. As an example, starch, a basic polysaccharide, becomes quite sticky (the opposite of slippery) and can possess significant binding qualities when hydrated, which is why starch is commonly used a glue. One therefore cannot assume that all polysaccharides are lubricious.

Furthermore, the Examiner has stated that Applicants have not defined the term “biomaterial” and therefore the Examiner considers biomaterial to be any material. The Examiner has once again placed upon the Applicants a burden to define each word used to describe the invention. Applicants are particularly perplexed given that the Examiner’s supervisor stated that if Applicants added the term “biomaterial” to the claims then the phrase would have structural characteristics and not simply be considered to be an intended use.² Obviously the Examiner’s Supervisor understood the term “biomaterial” to impart some limitation. The Applicants are not required to define each and every term used to describe there invention, but may instead rely on the plain meaning and knowledge of one of ordinary skill in the art.

The Examiner has made several other assumptions and statements regarding various claim terms. Applicants fully reserve the right to address each of these assumptions in a later filing in the present application or with regard to new claims in this or a later-filed application.

Fourth, and with regard to claim 34, the Examiner has taken the position that because the ceramic particles identified in the Staley et al. reference describe only a single dimension for the particles, they are inherently spherical. The position is factually incorrect. Both dictionary definition and geometric definitions clearly demonstrate that, even when an object is referred to as having a diameter, the object can take a variety of forms. For example, Merriam-Webster’s Collegiate Dictionary (10th Ed. 1996), defines “diameter” as “a chord passing through the center of a figure or body” and “the length of a straight line through the center of an object.” Similar definitions can also be found in Webster’s New Collegiate Dictionary (1981), for example. Furthermore, at least two basic geometric objects, namely as cylinders and cones, both have a defined diameter yet are not spherical. Still further, several of the prior art references cited by Applicants also refer to particles using a single dimension yet are clearly not spherical. For example, the Background of the Invention for the present application states:

² See May 5, 2004 Amendment and Reply Under 37 C.F.R. § 1.111, Page 10, lines 6-10.

R. A. Appell, "The Artificial urinary Sphincter and Periurethral Injections", Obstetrics and Gynecology Report. Vol. 2, No. 3, pp. 334-342, (1990), is a survey article disclosing various means of treating urethral sphincteric incompetence, including the use of injectables such as polytetrafluoroethylene micropolymer particles of about 4 to 100 microns in size in irregular shapes, with glycerin and polysorbate. (emphasis added) (Page 5, lines 4-12)

This is further evidence that reference to a single dimension does not require that an object be spherical. For all of these reasons, the mere recitation of a "diameter" does not inherently mean that a particle is a sphere, and Applicants submit that it is wholly improper for the Examiner to make such an assumption without additional supporting evidence.

The Examiner also has summarily declared that the Staley et al. reference teaches that metal and ceramic particles are inherently smooth and rounded.³ This statement also is incorrect. First, there is absolutely no place in the Staley et al. reference where this assertion is made, and the Examiner points to no particular location in the reference for this support. Second, much of the prior art previously addressed in related patent applications disclosed non-smooth and non-rounded ceramic particles, refuting the Examiner's position. For example, Page 4 of the present application refers to an article by Misiek et al. entitled "Soft Tissue Responses to Hydroxylapatite Particles of Different Shapes" which "discloses that the implantation of hydroxylapatite in the form of sharp edged particles or rounded particles in the buccal soft tissue pouches produced inflammatory response at the implant sites with both particle shapes." (emphasis added) (See Page 4, lines 9-16). This is just one example demonstrating that such particles are not necessarily smooth and rounded.

In an Advisory Action dated October 8, 2004, the Examiner commented that "even if the ceramic particles of Staley do not anticipate the limitations describing the particles, Staley also teaches spherical metal particles, which certainly do not have sharp or angular edges." This statement is both incorrect and irrelevant. First of all, in no location of the Staley reference is

³ Claim 34 previously did not mention the particles as being smooth. However, Applicants have amended claim 34 to now include this limitation.

there a teaching of a spherical metal particle, and the Examiner has completely failed to provide such support. As mentioned above, a reference to a single dimension does not inherently mean that an object is spherical, and in no other location of the reference is there even a hint of a spherical particle. Second, the teachings of the Staley et al. reference with regard to metal particles is completely irrelevant with regarding to claim 34, because claim 34 is directed to ceramic particles, not metallic particles.

Also in the October 8, 2004 Advisory Action, the Examiner attempted to uphold the rejection of claim 34 by stating that Applicants failed to define what constitutes a sharp and angular edge. In response to this rejection, Applicants once again direct the Examiner to the decision by the Board of Patent Appeals and Interferences dated July 26, 2001 for Interference No. 103,570. In particular, page 7 of the decision clearly shows that the Board fully considered Applicants' definition of the terms "rounded" or "smooth, rounded" and had no difficulty understanding the meaning of Applicants' definition while upholding the patentability of this feature. Applicants find it surprising that the Examiner has such difficulty with this term, particularly when the three-member Board did not have any difficulty with this definition.

For all of the above reasons, Applicants submit that the rejection of claim 34 is overcome.

In light of the number of issues that have been addressed in this Reply, Applicants believe that a telephonic or in-person interview may be beneficial to the final resolution of this matter. Therefore, Applicants respectfully request that the Examiner and the Examiner's supervisor contact the Attorneys for Applicants directly before any new Action is issued.

Applicants believe that the present application is now in condition for allowance. Favorable reconsideration of the application as amended is respectfully requested.


The Examiner is invited to contact the undersigned by telephone if it is felt that a telephone interview would advance the prosecution of the present application.

The Commissioner is hereby authorized to charge any additional fees which may be required regarding this application under 37 C.F.R. §§ 1.16-1.17, or credit any overpayment, to Deposit Account No. 06-1450. Should no proper payment be enclosed herewith, as by a check being in the wrong amount, unsigned, post-dated, otherwise improper or informal or even entirely missing, the Commissioner is authorized to charge the unpaid amount to Deposit Account No. 06-1450. If any extensions of time are needed for timely acceptance of papers submitted herewith, Applicants hereby petition for such extension under 37 C.F.R. §1.136 and authorizes payment of any such extensions fees to Deposit Account No. 06-1450.

Respectfully submitted,

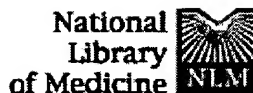
Date January 18, 2005

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Resorbable and nonresorbable hydroxyapatite granules as bone graft substitutes in rabbit cortical defects.

Liljensten E, Adolfsson E, Strid KG, Thomsen P.

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BACKGROUND: The use of various synthetic calcium phosphate compositions for the promotion of bone in bone defects is of potential interest because such materials may be tailor made and may bond to bone. There is yet an inadequate knowledge of the role of calcium phosphate composition and resorbability for the bone response.

PURPOSE: The aim of the present study was to compare the ability of resorbable versus nonresorbable hydroxyapatite (HA) granules to promote new bone formation in cortical bone defects. Resorbable and nonresorbable HA granules, used as bone graft substitutes, were evaluated after 6 weeks and 3 months in the rabbit tibia. Circular defects (diameter 5.0 mm) were made in both tibiae of 18 New Zealand white rabbits. The 36 defects were divided into three groups (six observations per group and time, respectively). The first group was augmented with resorbable HA granules, the second group was augmented with ceramic nonresorbable HA granules, and the third group was left without augmentation (control). The animals were killed after 6 weeks and 3 months, and the tissue was evaluated with light microscopic (LM) morphology and morphometry, scanning electron microscopy (SEM), and energy dispersive x-ray analysis (EDX).

RESULTS: After 3 months LM morphometry revealed significantly more newly formed bone in the two HA augmented groups compared with that in the control. A close contact was found between both kinds of HA granules and new bone as viewed with light microscopy and SEM. A relatively slow degradation process was indicated by the small reduction of the total granule area in the cortical defects. However, LM observations showed a change of granule form. Pilot experiments using SEM-EDX indicate that Ca and P contents had decreased in the resorbable HA granules between 6 weeks and 3 months. Further, a higher content of Ca and P was found in the newly formed bone close to granules, in comparison with more distant newly formed bone.

CONCLUSIONS: Our results suggest that both resorbable and nonresorbable HA granules promote new bone formation in rabbit

cortical defects, which does not occur in control defects.

PMID: 14536044 [PubMed - indexed for MEDLINE]

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EDITORS' CHOICE

edited by Gilbert Chin

OCEANOGRAPHY

Aqueous, not Aeolus

During glacial periods, the productivity in the Southern Ocean rises. This increase has been attributed to the greater availability of iron, which serves to fertilize the Southern Ocean. By drawing carbon dioxide from the atmosphere, the increased productivity feeds back positively, leading to an even cooler climate. According to the "iron hypothesis," the iron is delivered via dust blown into the ocean from arid regions, and Antarctic ice cores do indeed show more dust during glacial periods.

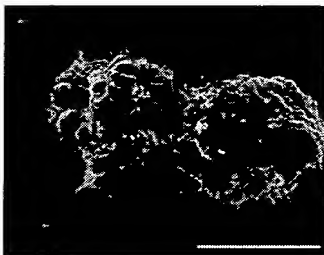
Latimer and Filippelli now offer evidence for a different source of the all-important iron. They have analyzed sediment cores from the South Atlantic and southern Indian Oceans to determine changes in sediment fluxes and productivity. During glacial times, productivity and iron fluxes are indeed higher, but most of the iron does not originate from eolian (wind-borne) dust. Rather, it is attributed to substantially increased weathering

and delivery of material from continental shelves, indicating that increases in productivity may have been fueled by upwelling. Therefore, eolian iron might have constituted a much smaller contribution than previously proposed. — JU
Paleoceanography, 10.1029/2000PA000586.

MICROBIOLOGY

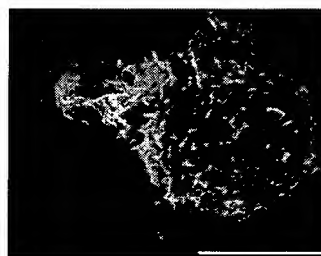
A Poison Capsule Defense

The soil fungus *Cryptococcus neoformans* can enter and persist within human macrophages, causing virulent infections if the person becomes immunocompromised. This fungus need not infect a vertebrate in order to complete its life cycle, so its pathogenicity is puzzling. A clue to its virulence may come from



its life in soil, where predatory microorganisms, such as amoebas, are present.

Steenbergen *et al.* have discovered remarkable parallels between the defensive strategies used by *C. neoformans* when eaten by *Acanthamoeba castellanii* and when surviving in human cells. Amoebas ingest the fungal cells, but the cells remain within vacuoles and produce a toxic polysaccharide, as they do when residing within macrophage vacuoles. The engulfed fungus possesses oth-



Amoebas (yellow) ingesting capsular *Cryptococcus* (red); bars, 10 μ m.

er unfriendly characteristics also exhibited during macrophage infection, and it ultimately kills its host amoeba,

whose death releases vital nutrients. Other soil fungi, such as *Histoplasma capsulatum*, that cause potentially fatal human infections are probably similarly armed because they, too, must run the gauntlet of voracious amoebas. — CA

Proc. Natl. Acad. Sci. U.S.A. 98, 15245 (2001).

PLANT SCIENCE

Early Decision Program

The initial cell division of the plant zygote produces an asymmetric outcome: the apical cell, from which most of the plant develops, and the larger basal cell that in part forms the suspensor, an embryonic tissue that anchors the developing embryo. Suspensor cells in the scarlet runner bean are particularly large and amenable to microdissection, and Weterings *et al.* have been able to identify two messenger RNAs that are specific to the suspensor cells and a third that is enriched in suspensor cells. These transcripts were not detected in the egg, but their asymmetric expression was apparent as early as the four-cell stage and may lead to clues about the molecular signals that establish the initial embryonic asymmetry. — PJH

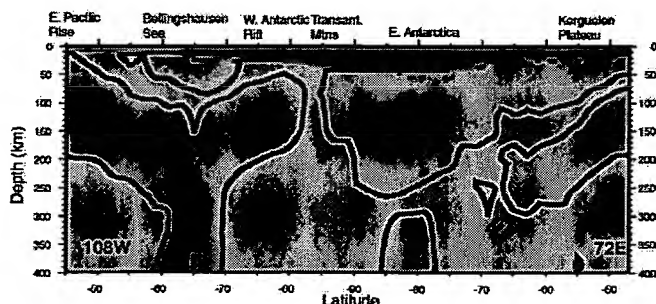
Plant Cell 13, 2409 (2001).

GEOPHYSICS

Reporting from the West Antarctic Rift

Our knowledge of the crust and upper mantle that lie under Earth's continents is poorest in the Southern Hemisphere, particularly beneath Antarctica. This region is important tectonically because Antarctica contains major crustal provinces and because rifting around Antarctica was instrumental in the formation of all of the major ocean basins. Recent volcanism and rifting may also be influencing the stability of the major ice sheets there.

Ritzwoller *et al.* have produced a new tomographic map of the upper mantle structure beneath Antarctica and the Southern Ocean using surface wave velocities. Their model implies that the mantle beneath eastern Antarctica transmits seismic waves rapidly (or is "fast") and thus is probably relatively cold and stiff. In contrast, the mantle beneath western Antarctica is "slower," and thus hotter, although not as slow as the regions at active, spreading ridges. This map is consistent with the presence of ongoing volcanism within a dormant rift zone. — BH



A west-east slice into Earth's interior (blue, fast; red, slow).

J. Geophys. Res., 10.1029/2001JB000179.

CHEMISTRY

Maintaining Mechanism

The replacement of volatile organic solvents with ionic liquids would reduce emissions of chemicals into the environment as well as promote energy-efficient separations. One concern, however, is that solvent interactions in an ionic medium may alter the mechanism (and hence the outcome) of classical organic reactions. Csihony *et al.* examined one workhorse reaction, the Friedel-Crafts acetylation of benzene, in an ionic liquid,

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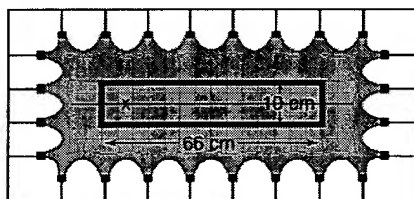
1-butyl-3-methylimidazolium chloride, with in situ infrared spectroscopy. They observed a temporal and spectral concordance of absorption bands associated with the expected intermediates for this reaction, such as the acetylium ion CH_3CO^+ in complex with the AlCl_4^- catalyst, for both the ionic solvent and a conventional organic solvent, 1,2-dichloroethane. — PDS

Green Chem. 3, 307 (2001).

MATERIALS SCIENCE

Bursting the Balloon

When a crack propagates through a solid, it typically takes a straight-line path, as this requires the least amount of work from the system. However, when a balloon is popped, it shatters into fragments that have wavy patterned edges. Deegan *et al.* have constructed an apparatus to study crack propagation in a controlled manner. A series of notches are cut into a rectangular sheet of rubber, and these are annealed to prevent fracture at these points. The projecting tabs are clamped, and the sample is then stretched in both directions, with the greater tension in the short direction of the sheet. Piercing the rubber with a pin generates a crack that propagates along the long direction. At low strains there is an initial kink in the crack, but usually it straightens, following the centerline of the sample. Above a critical strain, the crack oscillates



The strained rubber sheet.

around the centerline with a wavelength that depends on the strain values in both directions. The authors rule out stress-induced crystallization of the rubber and out-of-plane motions as the cause of the instability, and instead show that it can be characterized as a Hopf bifurcation. — MSL

Phys. Rev. Lett. 88, 014304 (2002).

ECOLOGY

The Decline of the Albatross

Populations of the wandering albatross species in the Southern Ocean have been declining for several decades. Commercial longline fishing for tuna ("by-catch") has been implicated in this decline; albatrosses often attempt to remove bait from fishing lines, the unsuccessful ones becoming en-

trapped themselves. However, because of the vast distances covered by albatrosses while foraging, it has proved difficult to establish the quantitative relationship between the distribution of longline fishing and albatross foraging.

Tuck *et al.* adopt a modeling approach to assess the impact of fishery by-catches on albatross populations, using 30-year data sets on albatross populations at two important breeding sites and parallel reported data on fishing activities in albatross foraging areas. The resulting simulations of albatross population dynamics appear to confirm a substantial impact of by-catch on one of the study populations (Crozet Islands), but indicate a less definite link with the observed population declines at the other (South Georgia). These models allow the integration of demographic and fishing data in a way that is impossible to achieve through direct observation, and, when developed further, will help to pinpoint regulatory and conservation priorities for the Southern Ocean. — AMS

J. Appl. Ecol. 38, 1182 (2001).

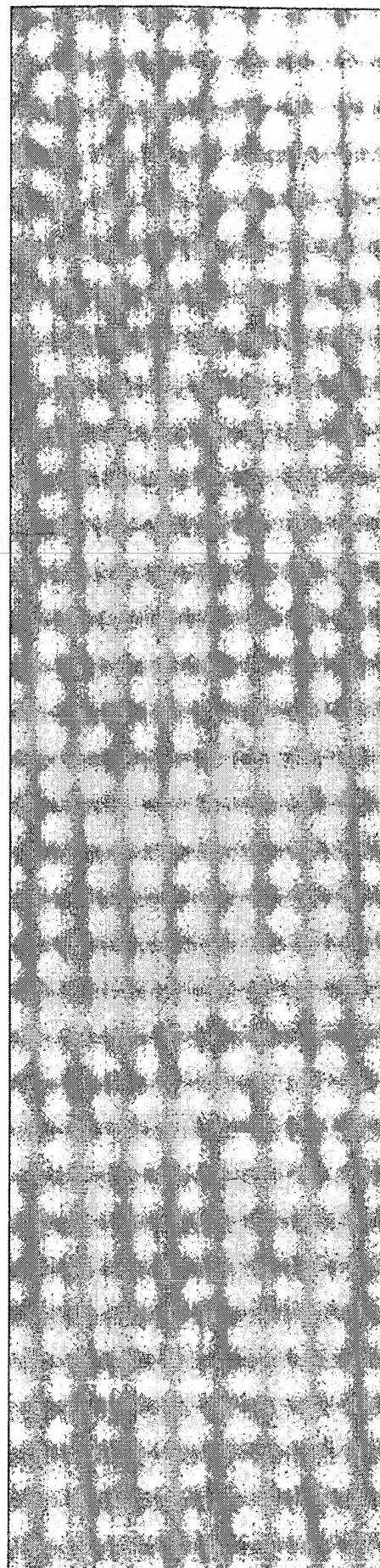
GENETICS

Contextual Analysis

Dopamine is a biogenic amine that functions as a neurotransmitter in central systems underlying behavior. Disturbances in dopaminergic pathways occur in many mental disorders, and the 7R allele of the human dopamine receptor gene *DRD4* has been associated with an elevated incidence of attention-deficit/hyperactivity disorder (ADHD). The 7R allele is one of many such alleles (2R-11R), all of which appear to contain integral multiples of a 48-base pair segment, with single-nucleotide polymorphisms in some of the tandem repeats.

Having sequenced and analyzed 600 *DRD4* alleles from a global sample, Ding *et al.* propose that the most common 2R-6R alleles all derive from single mutation or recombination events operating on an ancestral 4R allele. In contrast, the 7R allele, which itself could give rise to some of the less frequent alleles (5R-8R), would have required a series of at least four mutations and gene conversions. Further analysis suggests that the 7R allele may first have appeared about 40,000 years ago and subsequently been maintained due to positive selective pressure applied by the social and environmental conditions encountered during that watershed period, presumed to differ considerably from the present-day classroom where ADHD is found. — GJC

Proc. Natl. Acad. Sci. U.S.A. 99, 309 (2002).





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